Subretinal implantation of a monolayer of human embryonic stem cell-derived retinal pigment epithelium: a feasibility and safety study in Yucatan minipigs.

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Scientific Abstract:
PURPOSE: A subretinal implant termed CPCB-RPE1 is currently being developed to surgically replace dystrophic RPE in patients with dry age-related macular degeneration (AMD) and severe vision loss. CPCB-RPE1 is composed of a terminally differentiated, polarized human embryonic stem cell-derived RPE (hESC-RPE) monolayer pre-grown on a biocompatible, mesh-supported submicron parylene C membrane. The objective of the present delivery study was to assess the feasibility and 1-month safety of CPCB-RPE1 implantation in Yucatan minipigs, whose eyes are similar to human eyes in size and gross retinal anatomy. METHODS: This was a prospective, partially blinded, randomized study in 14 normal-sighted female Yucatan minipigs (aged 2 months, weighing 24-35 kg). Surgeons were blinded to the randomization codes and postoperative and post-mortem assessments were performed in a blinded manner. Eleven minipigs received CPCB-RPE1 while three control minipigs underwent sham surgery that generated subretinal blebs. All animals except two sham controls received combined local (Ozurdex dexamethasone intravitreal implant) and systemic (tacrolimus) immunosuppression or local immunosuppression alone. Correct placement of the CPCB-RPE1 implant was assessed by in vivo optical coherence tomography and post-mortem histology. hESC-RPE cells were identified using immunohistochemistry staining for TRA-1-85 (a human marker) and RPE65 (an RPE marker). As the study results of primary interest were nonnumerical no statistical analysis or tests were conducted. RESULTS: CPCB-RPE1 implants were reliably placed, without implant breakage, in the subretinal space of the minipig eye using surgical techniques similar to those that would be used in humans. Histologically, hESC-RPE cells were found to survive as an intact monolayer for 1 month based on immunohistochemistry staining for TRA-1-85 and RPE65. CONCLUSIONS: Although inconclusive regarding the necessity or benefit of systemic or local immunosuppression, our study demonstrates the feasibility and safety of CPCB-RPE1 subretinal implantation in a comparable animal model and provides an encouraging starting point for human studies.